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HL

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/837,459	04/18/97	MCKEE M	4995.0023

HM12/0805
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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1641	19

DATE MAILED: 08/05/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/837,459	Applicant(s) McKee et al
	Examiner Portner	Group Art Unit 1641

☒ Responsive to communication(s) filed on *Jun 4, 1999* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-55* is/are pending in the application.

Of the above, claim(s) *1-27 and 33-50* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28-32 and 51-55* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-55 are pending. claims 28-32 and 51-55 are under consideration..

Election/Restriction

1. In light of the traversal of the election/restriction made of record on paper number 14, it is here by vacated and claims 28-32 and 51-55 are under consideration as amended.

Please Note:

a. The amended claim 29 recites the limitations " said host bacteria is EHEC" is being interpreted by the examiner to mean that the composition of anti-intimin antibodies were raised against EHEC intimin rather than EPEC intimin as the instant specification does not teach a transformed strain of EHEC which carries both the EHEC and EPEC intimin sequences to which the antibodies were produced.

b. The phrase "block binding" is being read to mean either *partial* blocking or *complete* blocking of binding of the bacteria to a mammalian cell.

c. The phrase "antibodies specific for an intimin-expressing host bacteria" is being read to mean the native host or a recombinant host bacteria.

d. The claimed composition of claims 28-32 as now amended is being read to be a composition which comprises antibodies to EHEC or EPEC or EHEC and EPEC.

Rejections Maintained

Claim Rejections - 35 U.S.C. § 102

2. Claims 28, 31 , 51, 54 remain rejected under 35 U.S.C. 102(a) as being clearly anticipated by McKee, (May 1995) as applied to Claims 28 and 31 in paper number 11, for reasons of record.

3. Claims 28-32 and claims 51-55 remain rejected under 35 U.S.C. 102(b) as being anticipated by deAzavedo (CA2078716, March 22, 1994) with respect to antibodies to EHEC for reasons of record as applied to claims 28-32 and arguments made by the examiner in response Applicant below.

4. Claims 28-32 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Dougan et al (US Pat. 5,747,293)with respect to antibodies to EHEC and EPEC for reasons of record.

Response to Arguments

5. Arguments made of record with respect to rejections withdrawn will not be addressed herein.

6. McKee and O'brien (abstract B-5) is argued "to not teach or suggest antibodies which block binding of bacteria" nor do the antibodies cross react with both EHEC and EPEC.

7. Applicant's arguments filed with respect to McKee et al (two authors instead of three of the instant Application) have been fully considered but they are not persuasive because McKee et al do teach intimin specific polyclonal antibodies which reacted with both EHEC and EPEC using

the EHEC intimin fusion protein as an immunogen and the reference teaches that intimin is indicated as a primary adhesin. Therefore, the reference inherently teaches antibodies which are free from host cell antibodies because the immunogen was an affinity purified antigen and the antibodies evidenced the functional characteristic of specifically binding immunogenic epitopes of EHEC and EPEC and would therefore partially or fully block adhesin to mammalian cells as polyclonal antibodies are known to be produced to multiple epitopes present in an immunogenic molecule and the antibodies present in the polyclonal composition disclosed would be specific thereto and would interfere and therefore block binding to mammalian cells.

8. de Azavedo et al is argued to not teach or suggest all of the requirementsof Applicant's invention as now claimed, wherein it is asserted that deAzavedo believed that intimin was not sufficient for binding to mammalian cells and quotes deAzavedo as stating intimin is "necessary but not sufficient for the formation of the AE lesion".

9. Applicant's arguments filed with respect to deAzavedo have been fully considered but they are not persuasive because deAzavedo does teach that intimin is "associated with attaching and effacing activity of enterohemorrhagic E.coli" (page 10, lines 23-37; page 4, line 29) and states that "Both the EHEC and EPEC sequence show similarity to the Yersinia pseudotuberculosis invasin gene (Isberg, R.R et al (1987), Cell, Vol. 50, page 769) with greatest divergence at the C-terminal. The C-terminal end of the Yersinia inv gene is associated with receptor binding (Leong et al, EMBO J 1990, Vol. 6, pages 1979-1989) and it is possible **that the same applies to the**

eae gene products (emphasis added)." The patent claims antibodies both polyclonal and monoclonal to any epitope of the intimin protein of enterohemorrhagic E.coli (claims 13, dependent from claim 10; see page 22, lines 32-38) and teaches the production of antibodies to distinct epitopes in an unconserved region of the protein. In light of the sequence alignment of figure number 3 and the teaching at pages 10 (lines 35-38) and 11, lines 1-11) the reference clearly teaches the production of antibodies to the C-terminal of the antigen which is suggested to associated with receptor binding.

10. The examiner would like to point out that there is a difference in receptor binding and formation of the AE lesion. The formation of the AE lesion takes place through a series of steps, the first process step being receptor binding by intimin (known to be associated with attaching and effacing activity). Antibodies bound to intimin would be expected block the first step in the process of forming the AE lesion. Therefore, antibodies which specifically bound to intimin would also provide either partial or full blocking of binding to mammalian cells, especially if they were to the C-terminal of the protein as taught by deAzavedo.

11. Dougan is argued to drawn "to be of particular use in the detection of EHEC and EPEC.", that "there is no indication that such antibodies would block the binding of bacteria" and that intimin antibodies would not function in binding "and therefore teaches away from the use of intimin to produce useful antibodies."

12. Applicant's arguments filed with respect to Dougan have been fully considered but they are not persuasive because Dougan contrary to Applicant's assertion, teaches intimin "is a virulent factor that induces seroconversion in human volunteers" and teaches that "[T]he carboxy-terminal domain of this protein is able to bind to target cells". The reference goes on to teach that the disclosed antibodies are antibodies useful for treatment of EPEC infection (col. 2, lines 40-43) and therefore meets the claimed composition of antibodies which block binding (either partially or completely) and are immunoreactive with EPEC. The reference also suggest the generation of monoclonal antibodies which recognize C-terminal epitopes of EHEC intimin for the same purpose of treatment and/or detection of infection (col. 2, lines 45-52), as well as polyclonal antibodies to both the C-terminal of EPEC and EHEC (col. 2, lines 52-68) . The antibodies generated are reactive with wild type EPEC and are able agglutinate the bacteria due to surface expression of intimin (col. 7 and 8 before sequence listing.).

New Claim Limitations/New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. It is not clear how claim 29 further limits claim 28 with respect to EPEC as both EHEC and EPEC are recited in claim 28 and EHEC and EPEC strains are distinct one from another. EHEC produce shiga-like toxins and the sequence of intimin differs from that of EPEC though there are many conserved portions of the amino acid sequence of EHEC when compared to EPEC Clarification of what is intended by the new claim limitation is requested.

Claim Rejections - 35 U.S.C. § 102

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. Claims 51-55 are rejected under 35 U.S.C. 102(b) as being anticipated over deAzavedo. (as applied to claims 28-31)

17. deAzavedo teaches the production of antibodies, polyclonal and monoclonal, to both conserved (page 10, lines 23-37 and page 11, lines 1-11) and non-conserved (page 22, line 35 and (Figure 2)) regions of intimin. Amino acid sequence alignment is provided in Figure 3 which shows those regions of intimin which are conserved between EHEC and EPEC, immunogenic epitopes shared between EHEC and EPEC would produce antibodies, which are cross reactive and the production of both polyclonal and monoclonal antibodies are taught and claimed based upon the amino acid sequence of EHEC intimin (claims 13, dependent upon claim 10, see page 5, lines 8-11). Monoclonal antibodies are a type of monospecific antibody and meets the limitation of

antibodies which are affinity purified because the claimed composition of claim 55 is a product by process and a composition which reads on the claimed composition made by a materially different process anticipates the composition of claim 55 invention. If applicants contend that this is not the case, applicants are advised that the Office does not have the facilities for examining and comparing applicant's product with the prior art, and that the burden is on applicant to show a novel or unobvious difference between the claimed method and the method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. and Int.)

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

19. **Cravioto et al (1991)** is cited to show products of nature which are present in breast milk and block binding of EPEC to mammalian cells.

20. **Butterton et al (1995)** is cited to show an immunogenic composition which comprises the EaeA gene and shiga toxin I for the stimulation of antibodies against enterohemorrhagic Escherichia coli.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be changing February 7, 1998. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1641.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
July 26, 1999

JAMES C. HOUSEL 8/2/99
SUPERVISORY PATENT EXAMINER